Long-term results of ileal ureteric replacement: a 25-year single-centre experience

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Objective
To report the long-term outcomes of ileal ureteric replacement (IUR) in complex reconstruction of the urinary tract.

Patients and Methods
From 1991 to 2016, IUR was performed in 157 patients with structural or functional ureteric loss. In 52 patients, bilateral IUR became necessary. Implantation sites where either the native urinary bladder (n = 79) or intestinal reservoirs (n = 78). In the latter group, the technique was used at the time of primary urinary diversion (n = 34), in a secondary approach (n = 29), and in undiversion or conversion procedures (n = 15). Anti-refluxive implantation was performed in 37 patients. In eight patients the ileal ureter was implanted into the cutis as an ileal conduit. All patients were followed prospectively according to a standardised protocol.

Results
The mean follow-up was 54.1 months. In 114 patients with dilatation of the upper urinary tract before surgery a significant improvement of the dilatation was confirmed in 98 patients. Serum creatinine levels decreased or remained stable in 147 of the 157 patients. Reflux was present in all cases without and in six cases with an anti-reflux mechanism. In six patients, operative revision became necessary because of severe metabolic acidosis, mucus obstruction or stenosis of the ileal ureter.

Conclusions
To our knowledge, this is the world’s largest single-centre series of IUR reported to date. Long-term follow-up confirms that this approach is a safe and reliable solution, even under complex conditions. Anti-refluxive implantation is recommended for intestinal reservoirs, whereas reflux prevention seems to be of minor importance when the native bladder is chosen as the site of implantation.

Keywords
ileum, small intestine, ureteric replacement, urinary diversion, urinary reconstruction
the ureter was replaced simultaneously with primary urinary diversion due to lack of ureteric length and structural ureteric loss, mostly as a consequence of tumour infiltration or preoperative irradiation in 34 patients; in a secondary approach, as a solution for early or late complications of continent urinary diversion in 29 patients; and in combination with conversion or undiversion procedures in 15 patients, who presented with extremely short ureters after primary diversion. In all patients with intestinal reservoirs, new or additional bowel segments were excluded from the intestinal tract to bridge these defects (as all other solutions e.g. re-implantation of the native ureter in a modified Mathisen’s technique were not feasible), therefore representing additive IURs.

**Surgical Technique**

Ileal segments of appropriate length were isolated and anastomosed to either the renal pelvis or proximal ureteric stump in a simple end-to-end technique. For right-sided IUR, the creation of a mesenteric window is not necessary due to the topographic anatomy of the caecum and colon ascendens in relation to the ileal mesentery (Fig. 1A [2]); however, if left-sided IUR is planned, the ileal segment has to be brought into the retroperitoneal cavity through a mesenteric window in the colon descendens (Fig. 1B). Bilateral IUR was performed in 52 patients. For partial bilateral IUR, depending on the individual anatomical situation, the ureteric stumps were re-implanted into a common isoperistaltic ileal segment using an end-to-end and end-to-side technique (Fig. 1C). We avoid bowel tapering with subsequent risk of impaired perfusion and strictures by performing an adequate longitudinal incision (‘spatulation’) of the upper ureter, which allows easy adaptation of the ureteric stump to the ileal diameter.

For total bilateral ureteric replacement, the isoperistaltic ileal segment was subdivided into two appropriate parts. Both parts were then re-anastomosed in a ‘Y’ configuration for anastomosis to the renal pelvis preserving isoperistaltic direction (Fig. 1D).

Establishing the technique in manifold indications, reflux in patients with inevitable bacteriuria due to intestinal reservoirs was assumed to be potentially harmful to the upper urinary tract [3]. Mainly for this indication, anti-refluxive implantation was considered to be necessary and performed in 37 patients with 52 renal units (RUs), including 31 patients with an intestinal reservoir and also six patients with impaired renal function and the native bladder in situ by intussusception of the distal end of the ileal ureter (n = 35) or implantation into a serous-lined extramural tunnel (n = 2). Implantation of the ileal ureter without an anti-reflux mechanism was performed in 120 patients with 158 RU (including the eight patients with the IUR implanted into the cutis as an ileal conduit).

In the ensuing years, due to the low observed rates of pyelonephritis and no decrease in renal function, exclusively refluxive implantation of the ileal ureter was performed in patients with their native bladder in situ. All patients were followed according to a standardised protocol including analysis of serum creatinine and blood gases due to potential metabolic changes by incorporating bowel into the urinary tract. Regarding this matter, we do not recommend prophylactic bicarbonate use in IUR (as other authors do for intestinal reservoirs [3]), as the IUR itself is not supposed to store urine for long; however, if metabolic acidosis is observed in the follow-up period, we endorse further diagnostic evaluation (e.g. voiding function) and treatment with oral alkalising drugs. Additionally, monitoring of
vitamin B₁₂ levels is mandatory in the long-term setting, as IUR replacement often demands terminal ileum for reconstruction, which represents the primary site of vitamin B₁₂ resorption. Beside renal ultrasonography for morphological evaluation of the upper urinary tract and urine cytology, IVU or MRI urography were performed annually. Additionally, we routinely conduct diagnostic endoscopy of the urinary reservoir (native bladder and intestinal reservoir alike) and the IUR beginning at 5 years after surgery.

Results
An overview of our IUR cohort is shown in Table 1, with the data for the subgroup with the long-term follow-up (≥ 90 months) given in Table 2. There were no perioperative deaths. The mean (range) follow-up was 54.1 (1–219) months. In 136 RUs with preoperative dilatation there was a significant improvement radiographically in 115 RUs (84.6%), no change in 14 RUs (10.3%), and deterioration in seven RUs (5.1%). The serum creatinine level decreased or remained stable in 147 of the 157 (93.6%) patients. Reflux was detected in all patients without and in six (16%) with an anti-reflux-mechanism.

Metabolic Changes
The overall rate of metabolic hyperchloraemic acidosis in the patient cohort was 19.5%. In the group with native bladder it accounted for 18.9% and in the group with intestinal reservoirs for 20.1%. All patients were treated successfully with oral alkalisising drugs. In one patient with infravesical obstruction without elongation of the single ileal ureter, recurrent episodes of severe metabolic acidosis ceased completely after TURP.

Pyelonephritis
Recurrent pyelonephritis occurred in six of 65 patients (9.3%) with refluxive implantation into intestinal reservoirs. In two of these patients antibiotic medication could be stopped after 6 months, while three patients are still on low-dose oral antibiotic prophylaxis. In the subgroup of patients with native bladder and refluxive implantation of the ileal ureter, pyelonephritis occurred in 4.4% (three of 78 patients). There was no indication for long-term antibiotic prophylaxis in this patient group. In patients receiving an anti-refluxive implantation of the ileal ureter (n = 37), we observed pyelonephritis in two patients (5.4%) with their native bladder in situ and no pyelonephritis in patients with intestinal reservoirs.

Surgical Interventions
In our study group, six surgical interventions became necessary: two patients showed impaired renal function and recurrent episodes of severe metabolic acidosis 24 and 36 months after unilateral IUR. Extreme elongation and kinking of the ileal ureter required surgical revision with distal shortening of the ileal ureter. In one of the patients, mucous production with subsequent intermittent urinary stasis was a causal factor. Three further patients with recurrent mucous obstruction were treated endoscopically with spontaneous cessation of excessive mucous production 18 months after surgery. One other patient developed a significant stenosis of the ileal ureter 25 months after right-sided IUR for ureteric loss due to vascular prosthesis implantation, which required right-sided nephrectomy and complete excision of the ileal ureter. In further follow-up, the remaining RU of the patient maintained stable renal function with adequate drainage.

Specific Situations
One young patient with end-stage renal disease after several failed attempts to reconstruct bilateral megaureters and significant diuresis of dilute urine underwent conversion of an ileal conduit into a continent cutaneous ileocaecal reservoir in preparation for renal transplantation. This patient had not undergone renal transplantation in the following years mainly due to persisting non-compliance with therapy. In the long-term setting, one female patient with a single kidney lost her renal function 198 months after creation of an ileocaecal pouch and IUR (anti-refluxive implantation). She is currently awaiting allocation of an allograft.

Discussion
Schoemaker et al. [4] first reported ureteric reconstruction using intestinal segments in 1911. In recent decades, IUR has increasingly become established with good prognosis not adversely affecting renal function [5,6].

The safety of ileal ureters has been validated in several large series [7–12]. The largest series of ileal ureters to date was reported by Boxer et al. [7], which dates back to 1978, and documents reports of 94 ileal ureters in 89 patients, spanning 24 years from 1954 to 1978. The main causes of ureteric obstruction are still complications of open surgery or...
Table 2 Long-term results of IUR for the subgroup of patients with follow-up of ≥90 months.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Sex</th>
<th>Age at surgery, years</th>
<th>Indication / pre-existing CUR / undiversion</th>
<th>Underlying condition</th>
<th>Implantation</th>
<th>Undiversion / CUD / native bladder</th>
<th>Preoperative creatinine, mg/dL</th>
<th>Long-term creatinine, mg/dL</th>
<th>Dilatation of UUT</th>
<th>Acidosis / alkalisng drugs</th>
<th>Follow-up, months</th>
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<td>... with implantation into a pre-existing urinary reservoir</td>
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<tr>
<td>1</td>
<td>F</td>
<td>49</td>
<td>Obstruction</td>
<td>Meningomyelocele</td>
<td>Intussusception</td>
<td>MPI</td>
<td>3</td>
<td>1.8</td>
<td>Unchanged</td>
<td>Yes</td>
<td>219</td>
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<tr>
<td>2</td>
<td>M</td>
<td>33</td>
<td>Obstruction</td>
<td>Meningomyelocele</td>
<td>Intussusception</td>
<td>MPI</td>
<td>1.2</td>
<td>1</td>
<td>Improved</td>
<td>Yes</td>
<td>216</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>69</td>
<td>Obstruction</td>
<td>Urothelial carcinoma</td>
<td>Reflexive</td>
<td>MPI</td>
<td>1.2</td>
<td>1.5</td>
<td>Improved</td>
<td>No</td>
<td>92</td>
</tr>
<tr>
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<td>Urothelial carcinoma</td>
<td>Reflexive</td>
<td>MPI</td>
<td>1.1</td>
<td>1.3</td>
<td>Unchanged</td>
<td>No</td>
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<td>5</td>
<td>M</td>
<td>68</td>
<td>Obstruction</td>
<td>Urothelial carcinoma</td>
<td>Reflexive</td>
<td>MPI</td>
<td>1.2</td>
<td>1.2</td>
<td>Improved</td>
<td>Yes</td>
<td>92</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>55</td>
<td>Obstruction</td>
<td>Urothelial carcinoma</td>
<td>Reflexive</td>
<td>MPI</td>
<td>1.3</td>
<td>1.8</td>
<td>Improved</td>
<td>Yes</td>
<td>92</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>31</td>
<td>Obstruction</td>
<td>Neurogenic bladder dysfunction</td>
<td>Intussusception</td>
<td>MPI</td>
<td>0.6</td>
<td>0.6</td>
<td>Improved</td>
<td>No</td>
<td>149</td>
</tr>
</tbody>
</table>

... with simultaneous urinary diversion (ileoacaecal reservoir) | | | | | | | | | | | |
| 8          | M   | 64                    | Obstruction                               | Urothelial carcinoma | Intussusception | Orthotopic neobladder augmentation | 0.8 | 0.8 | Improved | No | 118 |
| 9          | F   | 15                    | Reflux VUR                                | Meningomyelocele     | Intussusception | Bladder augmentation | 0.7 | 0.7 | Unchanged | Yes | 106 |
| 10         | M   | 38                    | Obstruction                               | Neurogenic bladder dysfunction | Intussusception | Meningomyelocele | 0.6 | 0.9 | Improved | No | 97  |
| 11         | F   | 9                     | Obstruction                               | Ureteric megareter   | Reflexive       | MPI | 0.8 | 1   | Improved  | No  | 98  |
| 12         | F   | 6                     | Obstruction                               | Meningomyelocele     | Reflexive       | Meningomyelocele | 0.5 | 1   | Improved  | No  | 117 |

... in urinary conversion with implantation into a CUR | | | | | | | | | | | |
| 13         | M   | 58                    | Reflux                                   | Urothelial carcinoma | Reflexive       | Refluxive | 0.8 | 1.1 | Unchanged | No | 146 |
| 14         | M   | 63                    | Obstruction                               | Urothelial carcinoma | Intussusception | Bladder augmentation | 1.1 | 1.1 | Unchanged | No | 211 |

... with implantation into the native bladder | | | | | | | | | | | |
| 15         | F   | 27                    | Reflux VUR                                | Meningomyelocele     | Intussusception | MPI | 1.1 | 1.3 | Unchanged | No | 166 |
| 16         | M   | 23                    | Reflux VUR                                | Urothelial carcinoma | Intussusception | Meningomyelocele | 1.3 | 1.1 | Unchanged | No | 162 |

| M   | 48 | Obstruction   | Intussial cystitis | Reflexive | Native bladder | 1.1 | 1.2 | Unchanged | Yes | 165 |
| F   | 23 | Obstruction   | Stricture after ovarian abscess | Reflexive | Native bladder | 1.1 | 1.2 | Unchanged | Yes | 166 |
| TUR for urothelial carcinoma | Reflexive | Native bladder | 1.3 | 1.2 | Unchanged | No | 166 |
| TUR for urothelial carcinoma | Reflexive | Native bladder | 1 | 1 | Improved  | Yes | 158 |
| F   | 55 | IS Urolithiasis | Reflexive | Native bladder | 1.9 | 1.6 | Improved  | Yes | 139 |
| F   | 54 | IS Urolithiasis | Reflexive | Native bladder | 2 | 1.7 | Unchanged | No | 135 |
| F   | 19 | IS Urolithiasis | Reflexive | Native bladder | 1.7 | 1.2 | Improved  | No | 138 |
| F   | 51 | IS Urolithiasis | Reflexive | Native bladder | 1.3 | 1.1 | Improved  | No | 114 |
| F   | 64 | IS Urolithiasis | Reflexive | Native bladder | 0.7 | 0.7 | Improved  | No | 103 |
| F   | 49 | IS Irradiation (cervical cancer) | Reflexive | Native bladder | 0.7 | 0.7 | Improved  | No | 99  |
| M   | 73 | IS TUR for urothelial carcinoma | Reflexive | Native bladder | 1.3 | 1.2 | Improved  | No | 98  |
| M   | 66 | IS Urolithiasis | Reflexive | Native bladder | 1.4 | 1.4 | Improved  | No | 97  |
| F   | 55 | IS Irradiation (cervical cancer) | Reflexive | Native bladder | 1 | 0.8 | Improved  | No | 116 |
| M   | 65 | IS Urolithiasis | Reflexive | Native bladder | 1 | 1.5 | Improved  | No | 92  |
| F   | 34 | IS Irradiation (cervical cancer) | Reflexive | Native bladder | 0.7 | 0.8 | Improved  | No | 112 |
endoscopic interventions, Ormond’s disease or secondary retroperitoneal fibrosis after vascular surgery or radiotherapy for malignant pelvic disease. The increasing popularity of orthotopic bladder substitution and continent cutaneous intestinal reservoirs has recently created a new challenge for ureteric reconstruction in managing complex complications, as well as in conversion or undiversion procedures.

The safety assessment of IUR in the view of very long-term outcome includes considerations about renal function, the uretero–intestinal/vesico–intestinal anastomosis, mucus obstruction, recurrent upper UTIs and the risk of secondary malignancy, whereas long-term preservation of renal function has always been the principal issue in ureteric reconstruction.

Goodwin et al. [5] recommended the use of ≥15 cm of ileum to guarantee the best effect of unidirectional ileal peristalsis being an important mechanism for pyelonephritis prevention in the setting of IUR. These observations were confirmed by Thoeny et al. [13], who routinely used a 14–20 cm long, tubular isoperistaltic ileal segments as the afferent limb in orthotopic ileal neobladders. Vatandaslar et al. [14,15] concluded from their studies that neither tapering nor anti-refluxive implantation of the ileal ureter is necessary to preserve renal function.

In this context, the Monti technique [16,17] might have an advantage with lower rates of metabolic changes using short and re-configured bowel segments. However, compromised blood supply, especially at the end of a Monti-ureter, remains an additional risk for stricture occurrence. Consequently, reports of this technique in ureteric replacement are rare [18–20].

Considering our present cohort in the long-term setting, the need for anti-refluxive implantation of ileal ureters depends on several factors, including type of urinary reservoir and renal function as major decision points. As bacteriuria is inevitable in continent cutaneous urinary diversion and rectal reservoirs [3], here, in our opinion, anti-refluxive implantation seems necessary for preventing ascending pyelonephritis and subsequent loss of kidney function. The absence of pyelonephritis in this particular patient group in our present cohort strengthens this assumption. Additionally, in patients with decreased renal function, anti-refluxive implantation may decrease the risk of hyperchloremic metabolic acidosis by reducing the duration of contact of urine with the intestinal mucosa [21]. However, to date the necessity of anti-refluxive implantation is a subject of controversial discussion lacking definitive proofs for each implantation technique [15,21,22].

Our initial cohort was evaluated between 1991 and 2002 [1]; due to the retrospective character of this work and the fact
that our institution represents a tertiary referral centre, a considerable number of patients were lost to follow-up or died for other reasons. Consequently, a new follow-up cohort was evaluated including a long-term post-intervention period, therefore displaying the ‘real-life’ setting and evolution of our strategy over time. Within our reported cohort (Table 1), which represents the world’s largest single-centre experience of IUR, we evaluated the creatinine levels in a subgroup of 23 patients with a follow-up of ≥90 months (Table 2). Long-term renal function remained stable except for one patient with a single kidney, who developed end-stage renal impairment 198 months after creation of an ileocaecal pouch and IUR, mainly due to the specific underlying nephrological disease.

Because of the well-known tendency of ileum to elongate, its use is regarded as particularly critical in growing subjects and should therefore not be recommended. However, we successfully used distal intussusception in four and serous-lined extramural implantation of a pre-existing ileum conduit in one of the five patients aged <18 years to prevent reflux. With a mean (range) follow-up of 97.6 (72–135) months, none of these children and adolescents developed pyelonephritis or excessive elongation of their IUR. However, there was severe elongation of the ileal ureter in one adult patient with urodynamically confirmed subvesical obstruction. He had recurrent episodes of severe metabolic acidosis, which ceased completely after surgical intervention with adequate shortening of the ileal ureter and subsequent TURP; this case vividly demonstrates the need to monitor proper bladder emptying in these patients on a regular basis. Therefore, in preparation for an ileal ureter, it is mandatory to exclude any subvesical obstruction to prevent ileal elongation and possible metabolic consequences in the first place. As ileal segments continue to produce mucus after incorporation into the urinary tract, this occurrence can be troublesome when it interferes with upper urinary tract drainage or emptying the bladder or intestinal reservoirs. The risk of mucus obstruction can be reduced by using short ileal segments and providing complete drainage of the lower and upper urinary tract, avoiding residual urine and stasis [23]. While mucus obstruction with no identifiable cause can be managed endoscopically, morphological problems must be solved definitively, e.g. by shortening an elongated ureter.

In three patients excessive mucus production ceased spontaneously after 18 months and repeated endoscopic intervention. Progressive renal failure after ileal replacement of the ureter has been reported in patients with borderline renal function before surgery (serum creatinine >1.5 mg/dL [21]). However, serum creatinine alone is only weakly predictive of renal function after ureteric reconstruction with bowel. In the present series, the serum creatinine level decreased or remained stable in 147 of the 157 patients. Therefore, life-long surveillance of the upper urinary tract both functionally and structurally is mandatory.

In 136 RUs in patients with preoperative dilatation there was a significant improvement radiographically in 115 RUs (84.6%), no change in 14 RUs (10.3%), and deterioration in seven RUs (5.1%). The likelihood of metabolic changes after incorporating bowel into the urinary tract is strongly related to renal function [3]. The prevalence of hyperchloraemic acidosis after ileal ureteric replacement is significantly higher in patients with an impaired GFR [7]. In all, 15 patients with their native bladder in situ (18.9%) with mild hyperchloraemic metabolic acidosis needed permanent sodium bicarbonate administration.

Late uro-intestinal malignancy is a low but still a distinct risk in patients with incorporated bowel segments into their urinary tract [22]. To date, none of our present patients have developed malignant tumour growth in their reconstructed urinary tract. The patients presented here are routinely followed at 3–12-month intervals according to a standardised protocol including ultrasonography, analysis of serum creatinine and blood gases, as well as urine cytology. Depending on the serum creatinine level a conventional or MRI urography is taken once a year. Diuretic renography is added if these basic tests suggest obstruction, with periodic diagnostic endoscopy used from 5 years after surgery.

Conclusions

The present single-centre series, which represents the world’s largest series on the topic to date, confirms that IUR is a safe and reliable treatment option even in extremely complex cases. Refluxive implantation is not associated with a significantly increased rate of pyelonephritis in patients with their native bladder in situ as well as in orthotopic bladder substitutes; however, it is recommended in intestinal reservoirs based on our positive experience in this particular patient group.

As IUR has increasingly become established with good prognosis and no adverse effects on renal function, lifelong close surveillance is critical for the success of this procedure.

Acknowledgements

Arkadius Kocot and Daniel Vergho were involved in data acquisition. Arkadius Kocot, Charis Kalogirou and Daniel Vergho prepared the manuscript and Hubertus Riedmiller provided critical evaluation of the manuscript for scientific soundness and content. Charis Kalogirou drew Figure 1 and was involved in data processing.

Conflicts of Interest

None declared.
Ethical Standards
All the findings, data acquisition and processing, as well as the retrospective nature of this study comply with the ethical standards laid down in the latest declaration of Helsinki as well as with the statutes of the Ethics Committee of the University of Würzburg concerning retrospective medical studies.

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Abbreviations: IUR, ileal ureteric replacement; RU, renal unit.
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